On page 21, please replace the paragraph at lines 8-9 with the following heading: --Brief Description of the Drawing--.

On page 22, between lines 1 and 2, please insert the following heading: --Description of the Preferred Embodiments--.

IN THE CLAIMS

Kindly delete claims 1-12 and add the following new claims:

--14. (New) A method for the determination of TSH receptor autoantibodies (TSHR-autoAb) in a biological sample with the aid of a receptor binding assay, said method comprising the steps of:

(a) providing a solid phase carrying a recombinant human TSH receptor (rhTSHR) immobilized with the aid of a selective antibody against said human TSH receptor (anti-hTSHR-Ab), said rhTSHR being purified in the immobilized state by washing and thereby converted into an affinity-purified immobilized rhTSHR (rhTSHR(imm)*), and

A2

(b) determining the presence and/or amount of TSH receptor autoantibodies (TSHR-auto-Ab) in a biological sample in a two step assay comprising the steps of

(i) reacting said solid phase carrying the affinity-purified immobilized rhTSHR (rhTSHR(imm)*), optionally in the presence of a buffer solution, with a liquid biological sample to be assayed for the presence of said TSHR-auto-Ab to bind TSHR-auto-Ab present in said biological sample to said rhTSHR(imm)*,

(ii) separating the reacted solid phase from said liquid biological sample and, optionally, buffer solution, and washing said solid phase,

(iii) incubating said washed solid phase from step (ii) with a buffer solution comprising an amount of labeled bovine TSH (bTSH) for a sufficient time to occupy essentially all bTSH-binding sites of said rhTSHR(imm)* not occupied by TSHR-auto-Ab by reaction with said labeled bTSH, and

(iv) determining the presence and/or amount of said TSHR-auto-Ab to be determined in the biological sample on the basis of the amount of labeled bTSH bound to the solid phase.

15. (New) A method for the determination of TSH receptor autoantibodies (TSHR-auto-Ab) in a biological sample with the aid of a receptor binding assay, said method comprising the steps of

(a) providing a solid phase carrying a recombinant human TSH receptor (rhTSHR) immobilized with the aid of a selective antibody against the human TSH receptor (anti-hTSHR-Ab), said rhTSHR being purified in the immobilized state by washing and thereby converted into an affinity-purified immobilized rhTSHR (rhTSHR(imm)*), and

A2

(b) determining the presence and/or amount of TSH receptor autoantibodies (TSHR-auto-Ab) in said biological sample in a one step assay comprising the steps of

(i) reacting said solid phase carrying the affinity-purified immobilized rhTSHR (rhTSHR(imm)* with a single reaction solution prepared from the serum-containing biological sample to be assayed for the presence of TSHR-auto-Ab and a buffer solution containing an mount of labeled bovine TSH (bTSH) for a sufficient time to occupy essentially all bTSH-binding sites of the rhTSHR(imm)* not occupied by TSHR-auto-Ab by reaction with said labeled bTSH,

(ii) separating said reaction solution from said reacted solid phase and washing said solid phase, and

(iii) determining the presence and/or amount of the TSHR-auto-Ab to be determined in the biological sample on the basis of the amount of labeled bTSH bound to the solid phase.

16. A method according to Claim 14 or 15, wherein said solid phase is formed by the walls of test tubes which are precoated with an animal-specific antibody for binding the anti-TSHR-Ab.

17. A method according to either of Claim 14 or 15, wherein said selective antibody against the human TSH receptor (anti-hTSHR-Ab) is a monoclonal antibody (anti-hTSHR-mAb) which recognizes only conformational epitopes of the rhTSHR and is obtained by the technique of immunization an animal with a TSHR-DNA construct.

18. A method according to Claim 14 or 15, wherein said method is carried out in automated form, wherein said solid phase comprises suspended particles which are coated with a selective anti-hTSHR-Ab, and wherein the preparation of the rhTSHR and the sample are added in such a way that a sample solution containing said suspended solid particles and said rhTSHR preparation is temporarily formed.

19. A method according to Claim 14, wherein said labeled bTSH is added in step (b) (iii) in a serum-free buffer solution.

20. A method according to Claim 14 or 15, wherein step (b) (i) is carried out in the presence of at least one antibody against human TSH (anti-hTSH-Ab) which does not cross-react with bovine TSH.

21. A method according to either of Claims 14 or 15, wherein said TSH receptor autoantibodies (TSHR-auto-Ab) to be determined are receptor-stimulating autoantibodies whose occurrence in a human serum is characteristic of Graves' disease.

22. A method for the determination of TSH receptor autoantibodies (TSHR-auto-Ab) in a biological sample with the aid of a receptor binding assay, in which the sample is reacted with (i) a TSH receptor preparation (TSHR preparation) and (ii) labeled bovine TSH (bTSH), wherein the presence and/or amount of the TSHR-auto-Ab to be determined in the biological sample is determined on the basis of the bound amount of labeled bTSH in the complex, separated from the liquid phase, of bTSH or TSHR-auto-Ab, wherein the receptor binding assay is carried out as a two-step assay in a test

tube which is coated with an affinity-purified rhTSHR(imm)* or an immobilized fusion rhTSHR, in which assay:

(i) in the first step, a sample, which contains an added anti-hTSH antibody and a buffer are pipetted and incubated, the liquid phase is then removed from the test tube and the test tubes are washed and,

(ii) in the second step, a serum-free buffer solution which contains the labeled bTSH preparation is added to the test tube, the liquid phase is removed from the test tube after incubation for a sufficient period, the test tube is washed and the tracer bound to the walls of the test tube is measured.--

IN THE ABSTRACT OF THE DISCLOSURE

Please delete the present Abstract of the Disclosure and replace it with the following new Abstract of the Disclosure:

--Abstract of the Disclosure

Improved receptor assays for the detection of thyroid stimulating hormone receptor (TSHR) autoantibodies are described which use immobilized, affinity-purified rTSHR preparations as specific binders. This format, as well as novel measures for neutralizing pathologically increased human TSH (hTSH) levels in the sera, e.g., by the addition of anti-hHSH antibody, and/or eliminating the influence of anti-bovine TSH antibody, result in increased assay reliability and open up the possibility of preparing the assay constituents in a ready to use and/or well-standardized form for automatic processing and/or convenient marketing.--